

COMPLEMENT-FIXATION TITRES IN TERTIARY LYMPHOGRANULOMA VENEREUM *

A STUDY OF RESULTS AFTER TREATMENT WITH BROAD-SPECTRUM ANTIBIOTICS

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The diagnosis of lymphogranuloma venereum may sometimes present a problem, especially in the tertiary stage of the disease when clinical symptoms are indefinite or absent.

The laboratory aids in diagnosis are helpful, but are often difficult to interpret. The tissue pathology is not conclusive. In our experience the search for pathognomonic cells, inclusion bodies, and/or specific granules in tissue sections or exudate smears is of limited value. The isolation of the causative agent, while not difficult, is laborious, expensive, and not suitable for routine use.

The Frei test is more useful for exclusion of the disease than for diagnosis, and, as numerous authors have pointed out, it is apparently a permanent sensitivity. This makes for difficulty in determining whether a positive reaction relates to present or past infection. This is especially true in sections of the population which may show up to 40 per cent. positive reactions in random testing for skin sensitivity to the Frei antigen.

The complement-fixation test is of great value but, like other serological tests, it has limiting features. Because of the transitory nature of the initial lesion, it is seldom that a four-fold rise in antibody titre is demonstrated in paired sera of patients with lymphogranuloma venereum. Usually, by the time the first specimen has been obtained, the initial phase of the disease has subsided, and an elevated complement-fixation titre is observed. More often than not, the next specimen obtained from the patient does not show a significant four-fold rise in titre. Infection with other members of the psittacosis-lymphogranuloma venereum group of viruses must also be ruled out.

Knowledge of the titre and duration of complement-fixation antibodies in the sera of patients with lymphogranuloma venereum is relatively scanty. There are indications that the longer the patient has had the disease the higher will be the complement-fixation antibody titre of that patient's serum. This generalization is subject to individual variation, and we have seen patients with tertiary lymphogranuloma venereum who had comparatively low complement-fixation titres. The presence of complement-fixation antibodies in untreated cases may be of long duration. Greaves and Taggart (1953) have reported that in patients with asymptomatic lymphogranuloma venereum with a previous history of a bubo, the complement-fixation titres may persist for over a decade. It was thought that the circulating complement-fixation antibodies might be depressed after successful therapy, and, if so, this method could be useful for a more conclusive retrospective diagnosis of lymphogranuloma venereum.

We have previously presented clinical results of the use of the broad-spectrum antibiotics in the treatment of lymphogranuloma venereum (Banov, 1953, 1954; Banov and Goldberg, 1953). As part of the investigation, complement-fixation titres were carried out on the sera of some of the patients. The present report gives the results of the complement-fixation titres of cases of lymphogranuloma venereum treated with the broad-spectrum antibiotics.

Method

An attempt was made to determine the duration and height of the complement-fixation titres in the sera of patients who had clinical lymphogranuloma venereum (limited in this study to patients with

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TABLE
CLINICAL AND SEROLOGICAL FINDINGS IN FOURTEEN CASES OF LYMPHOGRANULOMA VENEREUM
BEFORE AND AFTER THERAPY

Case No.	Sex	Clinical Symptoms	Drug	Dosage (g.)	Titre			Clinical Results
					Before Therapy	After Therapy	Time (mths)	
1	F	Rectal stricture	Terramycin	15.5	1,280	80	27	Satisfactory
2	F	Rectal stricture	Terramycin	15	320	40	14	Satisfactory
3	F	Rectal stricture	Terramycin	14	640	40	20	Satisfactory
4	F	Rectal stricture	Terramycin	25	320	320	12	Satisfactory
5	F	Rectal stricture	Terramycin	25	320	320	16	Satisfactory
6	F	Rectal stricture	Terramycin	25	80	80	19	Questionable
7	F	Rectal stricture R-V fistula	Terramycin Erythromycin	25 15.6	1,280	320	23	Fistula persisted
8	F	Rectal stricture	Terramycin	25	80	80	16	Satisfactory
9	F	Rectal stricture	Aureomycin	3.75	80	Negative	12	Satisfactory
10	F	Rectal stricture	Aureomycin	3.75	320	320	13	Satisfactory
11	F	Rectal stricture	Chloramphenicol	10.5	20	Negative	24	Satisfactory
12	F	Rectal stricture	Chloramphenicol	26.5	640	320	22	Satisfactory
13	M	Rectal stricture	Chloramphenicol	30	640	640	22	Satisfactory
14	F	Rectal stricture	Chloramphenicol	21	320	160	17	Satisfactory

tertiary lymphogranuloma venereum with rectal strictures). These patients had given a positive complement-fixation titre before treatment and had been treated with various antibiotics with clinical success.

Fourteen patients with tertiary lymphogranuloma venereum (rectal involvement with subsequent formation of rectal strictures) were treated with one of the following antibiotics: terramycin, chloramphenicol, aureomycin, and erythromycin. One patient (Case 7) received treatment with terramycin and erythromycin combined. The patients were followed for periods of 12 to 27 months after therapy and the complement-fixation titres of their sera were determined. Thirteen of these patients were Negro women and the other was a Negro boy. All received a complete physical examination and routine laboratory investigation. In each case a biopsy was performed to rule out rectal carcinoma.

Because there are no satisfactory laboratory criteria for determining adequacy of treatment of the individual case, the following clinical criteria have been evolved and employed at this clinic.

Patient's Observations

- (1) Absence of rectal bleeding.
- (2) Diminution of straining at stool.
- (3) Reduction of pain at defaecation.
- (4) Absence of mucus and purulent exudate from the rectum.

Physician's Observations

- (1) Rectal wall and stricture changed to lining of smooth, grey appearance.
- (2) Apparent evidence of larger lumen of rectal stricture.

The usual 100 per cent. complement-fixation test with overnight icebox incubation was used. The antigen employed was Lygranum*. All comparable

titres were obtained from matched specimens; that is, the titrations on the pre-therapy specimen of serum from each patient were performed at the same time, using the same batch of reagents. The sera were stored at -20°C . The titres are expressed as reciprocals of the highest dilution of serum which gave 3+ or 4+ fixation of complement.

Results

The results obtained are outlined in the Table. It will be seen that in fourteen sets of paired sera seven showed no significant change in titre and seven showed a four-fold decrease in titre. However, in these latter paired sera, four of the seven, while showing a decrease in titre, still had residual titres of 1:40 or higher. It is generally agreed that a lymphogranuloma venereum titre of 1:40 is within the significant range and is indicative of a present or previous infection with the virus. Of the fourteen patients, twelve still had circulating antibodies to a significant titre, some as long as 27 months after apparently successful antibiotic treatment. Only two patients showed no complement-fixation antibodies after therapy.

Discussion

We believe that these serological findings of tertiary lymphogranuloma venereum should be interpreted in a manner similar to that of a Frei test. Positive reactions, even to a titre as high as 1:640, do not necessarily indicate an active infection of the patient with the virus, in so far as the activity of the virus may be judged by clinical symptoms.

The laboratory results also indicate that the amount of antibiotic necessary to halt the clinical manifestations of lymphogranuloma venereum is usually not sufficient to stop antibody formation against the virus particles even after 2 years. This

* Lygranum was obtained from E. R. Squibb & Sons.

may suggest that active virus particles are still present after successful clinical therapy and may partially explain the large number of supposed re-infections observed in this disease.

Summary

Patients with tertiary lymphogranuloma venereum continue to maintain circulating complement-fixation antibodies against the virus for as long as 27 months, even after clinically satisfactory anti-

biotic therapy. Diminishing complement-fixation titres cannot be used to establish a retrospective diagnosis of the disease even after clinically successful treatment with the broad-spectrum antibiotics.

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